

A SIMULATION STUDY OF MECHANISM OF POSTFLIGHT ORTHOSTATIC INTOLERANCE

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Abstract The aim of this study was to investigate the role played by the factors, such as altered vasoreactivity of resistance vessels in different body regions, and depressed cardiac contractility in the genesis of postflight cardiovascular dysfunction. The model we used is based on the model developed by Mechior et al. (1994) with modification by incorporating into the model, some more detailed sub-models to describe blood redistribution, cardiac contractility, local vascular tone changes, and baroreflex control mechanism. The simulated cardiovascular response to LBNP, HUT, and +Gz(low level) stresses have been shown to compare well with the relevant experimental data. Further computer simulation studies were performed to assess the contributions of each factor on cardiovascular dysfunction postflight. The simulation demonstrated that both the hypovolemia and depressed cardiac contractility elicit obvious changes in cardiovascular responses to orthostatic stress. Although an increase in vasoconstrictor responsiveness of brain vessels does not elicit significant changes for the main hemodynamic variables, the cerebral blood flow is decreased dramatically. However, if the vasoreactivity of brain vessels kept unchanged, the decrease in vascular tone of vessels in lower body does not cause significant changes in cerebral blood flow.

Key words Cardiovascular system, computer simulation, weightlessness

I. INTRODUCTION

Orthostatic intolerance (OI) following exposure to microgravity or head-down bed rest is frequently observed and is thought to be multifactorial origin[1,2]. Although hypovolemia is considered as the primary cause of OI, the role played by other factors, such as the lowered vasoconstrictor responsiveness (VCR) of resistance vessels, the enhanced vasoconstriction response of cerebral vessels, and the depressed myocardial contractility need to be elucidated[3,4]. It is difficult to assess experimentally how each of these changes would affect orthostatic tolerance and how these factors interact with each other. An alternative

approach is to conduct simulation studies by use of mathematical models of cardiovascular system (CVS) capable of simulating the CVS response to orthostatic stress. This presentation describes the construction of the model used, and presents the preliminary simulation results illustrating the effects of varying individually the level of hypovolemia, VCR of the resistance vessels in lower limbs and abdominal viscera, VCR of the brain vessels or myocardial contractility on responses to orthostatic stress. The ultimate goal of our work was to integrate the new experimental findings and to simulate the complexity to get a thorough understanding of the mechanism of postflight cardiovascular dysfunction and orthostatic intolerance.

II. METHOD

1) Model Description Based on the previous work of Melchior et al[5], we have developed a mathematical model by incorporating some more detailed sub-models to describe blood redistribution, cardiac contractility, peripheral circulation, local vascular tone changes, and baroreflex control mechanism[6,7] (Fig. 1). Here we briefly review the main points of the model. More detailed descriptions of the model have been given in previous work [6, 7]

Because the arteries and capillaries are much less compliant than the veins, we assumed that blood volume redistribution during LBNP takes place only in the venous beds. Venous blood volume is considered to be stored in seven different compartments representing the head and up-limbs (HUL), thoracic region (THO), abdomen region (ABD), pelvis and buttocks (PB), thigh (THI), calf (CAL) and foot (FT). We considered the phenomena of collapse of venous vessels during negative transmural pressure and employed two tangent functions to describe the P-V relations of each compartment.

$$\Delta V_i = \begin{cases} \frac{2\Delta V_{i m+}}{\pi} \cdot \arctan\left[\frac{\pi}{2} \cdot C_{i0} \cdot \frac{\Delta P_{i trans}}{\Delta V_{i m+}}\right] & (\Delta P_{i trans} > 0) \\ \frac{2\Delta V_{i m-}}{\pi} \cdot \arctan\left[\frac{\pi}{2} \cdot C_{i0} \cdot \frac{\Delta P_{i trans}}{\Delta V_{i m-}}\right] & (\Delta P_{i trans} < 0) \end{cases}$$

where $i = \text{HUL, THO, ABD, PB, THI, CAL and FT}$; C_{i0} is

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the compliance for the small variations of $\Delta V_{i trans}$, ΔV_{im+} and ΔV_{im-} are the maximal increment and decrement of each compartment.

$$\Delta CVP = \lambda \cdot [\exp(\beta \cdot V_{LVED}) - \exp(\beta \cdot V_{0LVED})]$$

where λ is a constant and β is left ventricular elastic stiffness.

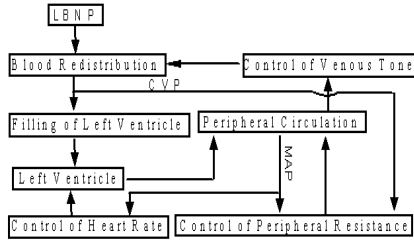


Fig1 Block diagram of the cardiovascular model

The heart rate and venous tone are modulated by the carotid baroreceptors, whereas the peripheral resistance is regulated by both carotid and cardiopulmonary baroreceptors. The model was validated for simulation of the CVS response to exposure of LBNP, or HUT by the data obtained from human experiment and published data [6, 7].

2) Simulation Procedure By use of the developed model, CVS responses to LBNP were simulated separately for each of the four kinds of physiologic changes that occurred in the simulated subject. The changes were: 1) decrease of blood volume; 2) 12% decrease of blood volume plus decrease of VCR of resistance vessels in abdominal viscera and lower limbs; 3) 12% decrease of blood volume plus 30% decrease of VCR of resistance vessels in lower

We used the work of Melchior et al.[5] to correlated ΔCVP and left ventricular end-diastolic volume (VLVED) during LBNP, then

limbs and abdominal viscera plus enhanced vasoconstriction of cerebral vessels; 4) 12% decrease of blood volume combined with decrease of myocardial contractility. The simulation model was programmed with MATLAB language and implemented in an IBM compatible personal computer.

III. RESULTS

1) Effects of blood volume decrease The more decrease of blood volume, the more changes will be (fig 2). If the amount of the decrease of blood volume is less than 5% of the total blood volume, HR and BP can be completely maintained in their physiological range by the regulation of baroreflex during orthostatic stress exposure. If the amount of the decrease of blood volume is more than 15% of the total blood volume, the hemodynamic variables can be in normal range when the simulated subject is in supine and at rest. However, the BP falls steeply and CVS might collapse with orthostatic stress (even if the intensity of the stress is relatively low). Shock Index (SI, $SI = HR/SBP$) will be greater than 1.0 (no shock occurs) during LBNP stresses if the decrease of blood volume is more than 15% of the total blood volume.

2) Effects of decrease of VCR of resistance vessels in lower body Simulation results indicated that the decrease of VCR of resistance vessels in lower body affected insignificantly on HR and BP during LBNP exposure.

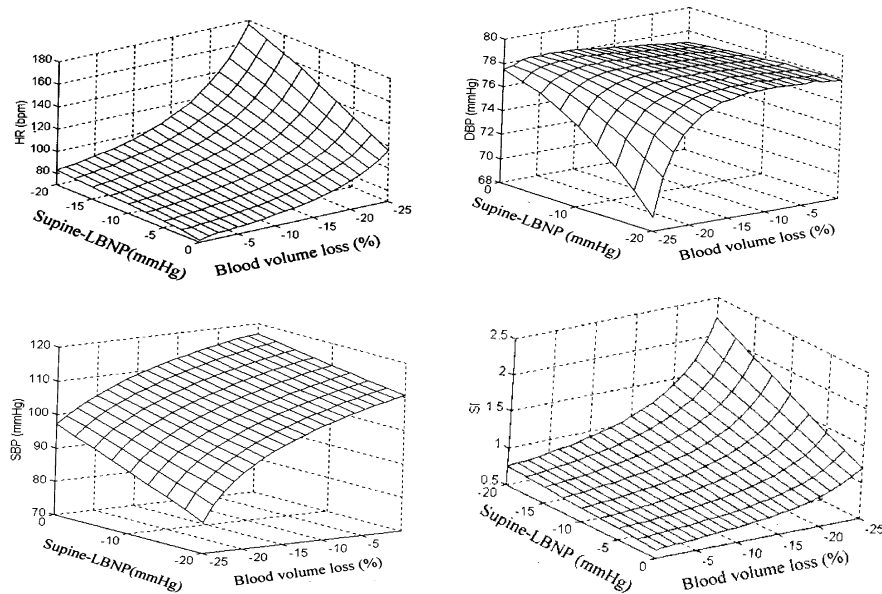


Fig2 Effects of hypovolemia on HR, BP and Shock Index response to supine LBNP

3) Effects of enhanced vasoconstrictor of cerebral vessels The simulation results suggested that the enhanced vasoconstriction response of cerebral vessels result in a significant decrease of cerebral blood flow velocities, although it did not elicit obvious changes in HR and BP (fig 3).

4) Effects of depressed myocardial contractility Significant increase of HR and decrease of BP can be seen when cardiac contractility is depressed (Tab 1).

Table 1 Effect of depressed myocardial contractility (ΔMC) on CVS response to LBNP (-50mmHg)

ΔMC (%)	HR (bpm)	SBP (mmHg)	DBP (mmHg)	CO (L/min)
0	131	93	76.1	4.15
-10	139	90	75.2	3.88
-20	150	88	72.3	3.66

As shown in Fig 4, the augment of HR is increased significantly as LBNP and myocardia contractility is decreased. The decrement of SBP is reduced progressively with the decrement of myocardia contractility. However, DBP is increased slightly when myocardia contractility is decreased slightly with low level LBNP. But if the decrement of myocardia contractility is over 10%, DBP decreases

sharply with the increment of LBNP exposure, and the system seemed to run into collapse. Also CO is decreased with the decrement of myocardia contractility and increment of LBNP. It is obvious that CO tends to a steady level when both the decreases of myocardia contractility and LBNP are high.

IV. DISCUSSION

Our simulation results show that both the hypovolemia and depressed myocardial contractility might elicit obvious changes in cardiovascular responses to orthostatic stress. Although an increase in vasoconstrictor responsiveness of brain vessels does not elicit significant changes for the main hemodynamic variables, the cerebral blood flow is decreased dramatically. However, if the vasoreactivity of brain vessels kept unchanged, the decrease in vascular tone of vessels in lower body would not cause significant changes in cerebral blood flow. These results suggest that the role of changes of vasoreactivity in the OI need to be further elucidated. What we presented is a preliminary result. Further improvement of the present model is needed to incorporate subsystems describing the adaptive changes, hemodynamics, heart performance, and regional circulation during microgravity base on new experimental findings.

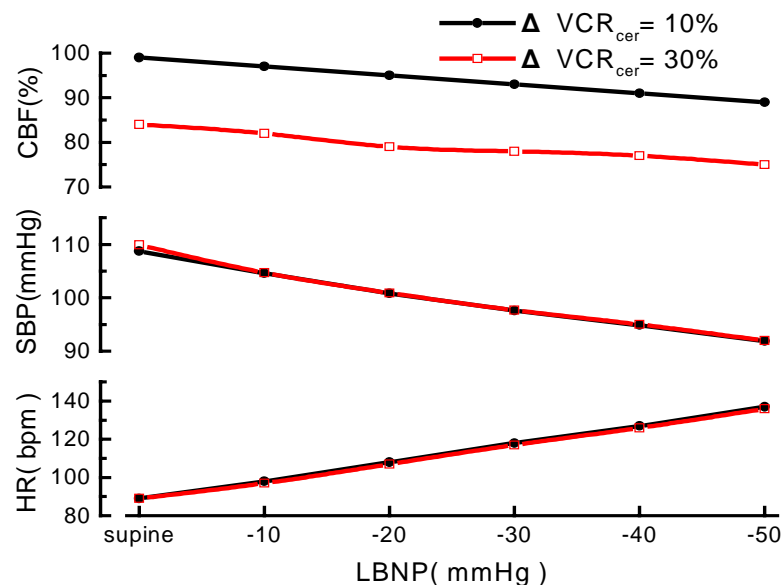


Fig3 Effect of enhanced vasoconstriction of cerebral vessels on CBF, BP and HR response to supine LBNP

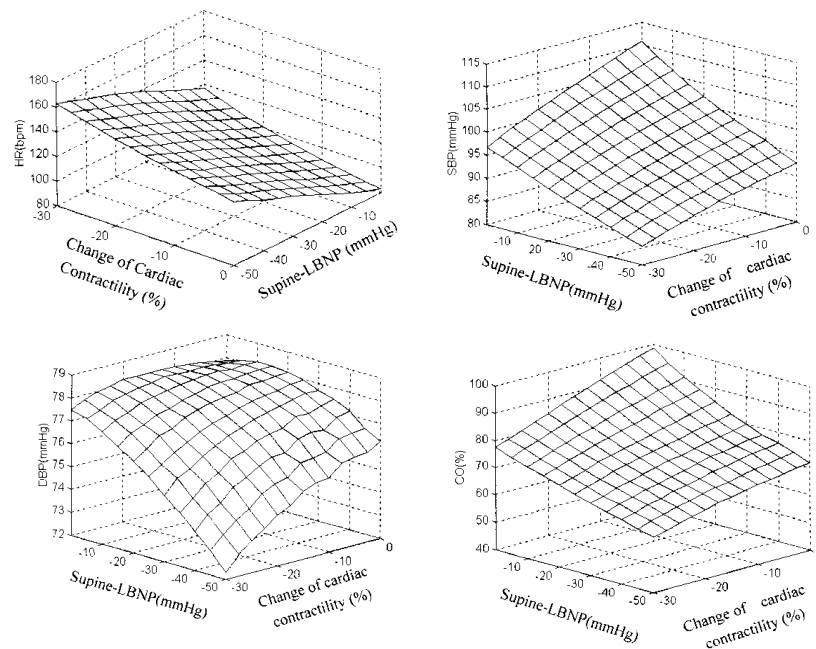


Fig4 Effect of depression of myocardial contractility on HR, SBP, DBP and CO response to supine LBNP

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